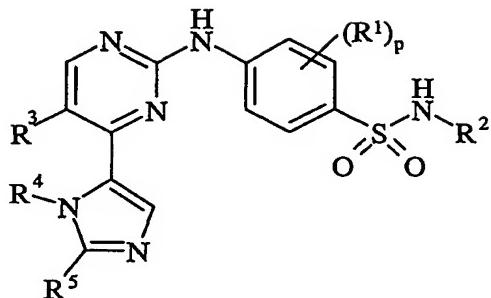


Claims

1. A compound of formula (I):



5

(I)

wherein:

**R<sup>1</sup>** is halo, cyano, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxy;

**p** is 0-2; wherein the values of R<sup>1</sup> may be the same or different;

**R<sup>2</sup>** is hydrogen, C<sub>1-4</sub>alkyl, C<sub>2-4</sub>alkenyl, C<sub>2-4</sub>alkynyl, C<sub>3-6</sub>cycloalkyl,

10 C<sub>3-6</sub>cycloalkylC<sub>1-3</sub>alkyl, a heterocyclyl or heterocyclylC<sub>1-3</sub>alkyl; wherein R<sup>2</sup> may be optionally substituted on carbon by one or more hydroxy, methyl, ethyl, methoxy, ethoxy, propoxy, trifluoromethyl, trifluoromethoxy, 2,2,2-trifluoroethoxy or cyclopropylmethoxy; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by one or more methyl, ethyl, acetyl, 2,2,2-trifluoroethyl or methoxyethyl;

15 **R<sup>3</sup>** is hydrogen, halo or cyano;

**R<sup>4</sup>** is C<sub>1-6</sub>alkyl or C<sub>1-6</sub>alkoxyC<sub>1-6</sub>alkyl;

**R<sup>5</sup>** is substituted methyl, optionally substituted C<sub>2-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl or optionally substituted C<sub>2-6</sub>alkenyl; wherein said substituents are selected from one or more hydroxy, methoxy, ethoxy, propoxy, isopropoxy, trifluoromethyl, trifluoromethoxy, 2,2,2-

20 trifluoroethoxy, phenyl, methylamino, ethylamino, dimethylamino, diethylamino, methylthio, ethylthio, propylthio, isopropylthio, methylsulphanyl, ethylsulphanyl, propylsulphanyl, isopropylsulphanyl, methylsulphonyl, ethylsulphonyl, propylsulphonyl, isopropylsulphonyl or cyclopropylmethoxy;

or a pharmaceutically acceptable salt or an *in vivo* hydrolysable ester thereof;

25 provided that the compound is not 4-(1-methyl-2-ethylimidazol-5-yl)-2-{4-[N-(tetrahydrofuran-2-ylmethyl)sulphamoyl]anilino}pyrimidine; 4-(1-methyl-2-ethyl-imidazol-5-yl)-2-{4-[N-(2-methoxyethyl)sulphamoyl]anilino}pyrimidine; 4-(1-methyl-2-isopropyl-imidazol-5-yl)-2-{4-

[N-(2-methoxyethyl)sulphamoyl]anilino}pyrimidine; 4-(1-methyl-2-isopropyl-imidazol-5-yl)-2-{4-[N-(cyclopropylmethyl) sulphamoyl]anilino}pyrimidine; 4-(1-methyl-2-isopropyl-imidazol-5-yl)-2-{4-[N-(tetrahydrofur-2-ylmethyl)sulphamoyl]anilino}pyrimidine; 4-(1-methyl-2-ethylimidazol-5-yl)-2-{4-[N-(cyclopropylmethyl) sulphamoyl]anilino}pyrimidine; 4-

5 (1-methyl-2-ethyl-imidazol-5-yl)-2-[4-(N-cyclopropylsulphamoyl) anilino]pyrimidine; 4-(1-methyl-2-ethylimidazol-5-yl)-2-[4-(N-cyclobutyl-sulphamoyl) anilino]pyrimidine; or 4-(1-methyl-2-methoxymethylimidazol-5-yl)-2-{4-[N-(2-methoxyethyl)sulphamoyl]anilino}pyrimidine.

10 2. A compound of formula (I) according to claim 1 wherein p is 0; or a pharmaceutically acceptable salt or an *in vivo* hydrolysable ester thereof.

3. A compound of formula (I) according to either claim 1 or claim 2 wherein R<sup>2</sup> is hydrogen, C<sub>1-4</sub>alkyl, C<sub>2-4</sub>alkenyl, C<sub>3-6</sub>cycloalkyl, C<sub>3-6</sub>cycloalkylC<sub>1-3</sub>alkyl or heterocyclylC<sub>1-3</sub>alkyl; wherein R<sup>2</sup> may be optionally substituted on carbon by one or more hydroxy, methoxy, ethoxy or trifluoromethyl; or a pharmaceutically acceptable salt or an *in vivo* hydrolysable ester thereof.

20 4. A compound of formula (I) according to any one of claims 1-3 wherein R<sup>3</sup> is hydrogen; or a pharmaceutically acceptable salt or an *in vivo* hydrolysable ester thereof.

25 5. A compound of formula (I) according to any one of claims 1-4 wherein R<sup>4</sup> is C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkoxyC<sub>1-4</sub>alkyl; or a pharmaceutically acceptable salt or an *in vivo* hydrolysable ester thereof.

6. A compound of formula (I) according to any one of claims 1-5 wherein R<sup>5</sup> is substituted methyl, optionally substituted C<sub>2-6</sub>alkyl; C<sub>3-6</sub>cycloalkyl or optionally substituted C<sub>2-6</sub>alkenyl; wherein said substituents are selected from one or more hydroxy, methoxy, ethoxy, isopropoxy, phenyl, ethylamino, dimethylamino, methylthio, ethylthio, isopropylthio, ethylsulphinyl or ethylsulphonyl; or a pharmaceutically acceptable salt or an *in vivo* hydrolysable ester thereof.

7. A compound of formula (I) as depicted in claim 1 wherein:

p is 0;

R<sup>2</sup> is hydrogen, 2-ethoxyethyl, 2-methoxyethyl, 2-hydroxyethyl, 2,2,2-trifluoroethyl, 3-methoxypropyl, t-butyl, allyl, cyclopropyl, cyclobutyl, cyclopropylmethyl or tetrahydrofur-2-ylmethyl;

R<sup>3</sup> is hydrogen;

R<sup>4</sup> is methyl, ethyl, propyl, isopropyl or 1-methoxyprop-2-yl; or

R<sup>5</sup> is methoxymethyl, 2-methoxyethyl, 2-hydroxy-2-methylpropyl, propyl, isopropyl, ethyl, butyl, isobutyl, cyclopropyl, 2-methyl-1-propenyl, 3-but enyl, 1-propenyl, 3,3-dimethylbutyl, phenethyl, dimethylaminomethyl, ethylaminomethyl, ethoxymethyl, methylthiomethyl, isopropylthiomethyl, ethylthiomethyl, ethylsulphinlmethyl, ethylsulphonylmethyl or isopropoxymethyl;  
or a pharmaceutically acceptable salt or an *in vivo* hydrolysable ester thereof;  
provided that the compound is not 4-(1-methyl-2-ethylimidazol-5-yl)-2-{4-[N-(tetrahydrofur-2-ylmethyl)sulphamoyl]anilino}pyrimidine; 4-(1-methyl-2-ethyl-imidazol-5-yl)-2-{4-[N-(2-methoxyethyl)sulphamoyl]anilino}pyrimidine; 4-(1-methyl-2-isopropyl-imidazol-5-yl)-2-{4-[N-(2-methoxyethyl)sulphamoyl]anilino}pyrimidine; 4-(1-methyl-2-isopropyl-imidazol-5-yl)-2-{4-[N-(cyclopropylmethyl) sulphamoyl]anilino}pyrimidine; 4-(1-methyl-2-isopropyl-imidazol-5-yl)-2-{4-[N-(tetrahydrofur-2-ylmethyl)sulphamoyl]anilino}pyrimidine; 4-(1-methyl-2-ethylimidazol-5-yl)-2-{4-[N-(cyclopropylmethyl) sulphamoyl]anilino}pyrimidine; 4-(1-methyl-2-ethyl-imidazol-5-yl)-2-[4-(N-cyclopropylsulphamoyl) anilino]pyrimidine; 4-(1-methyl-2-ethylimidazol-5-yl)-2-[4-(N-cyclobutyl-sulphamoyl) anilino]pyrimidine; or 4-(1-methyl-2-methoxymethylimidazol-5-yl)-2-{4-[N-(2-methoxyethyl)sulphamoyl]anilino}pyrimidine.

25

8. A compound of formula (I) as depicted in claim 1 selected from:

4-(1,2-diethylimidazol-5-yl)-2-{4-[N-(2-ethoxyethyl)sulphamoyl]anilino}pyrimidine;

4-(1-isopropyl-2-methoxymethylimidazol-5-yl)-2-{4-[N-(2-ethoxyethyl)sulphamoyl]anilino}pyrimidine;

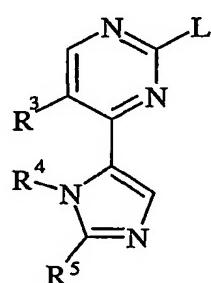
30 4-(1,2-diethylimidazol-5-yl)-2-{4-[N-(cyclopropyl)sulphamoyl]anilino}pyrimidine;

4-(1,2-diethylimidazol-5-yl)-2-{4-[N-(allyl)sulphamoyl]anilino}pyrimidine;

4-(1-isopropyl-2-cyclopropylimidazol-5-yl)-2-{4-[N-(2-methoxyethyl)sulphamoyl]anilino}pyrimidine;

- 4-(1-methyl-2-propylimidazol-5-yl)-2-{4-[N-(2-ethoxyethyl)sulphamoyl]anilino}pyrimidine;  
 4-(1-ethyl-2-propylimidazol-5-yl)-2-{4-[N-(2-methoxyethyl)sulphamoyl]anilino}pyrimidine;  
 4-(1-isopropyl-2-propylimidazol-5-yl)-2-{4-[N-(2-methoxyethyl)sulphamoyl]anilino}  
 pyrimidine;
- 5    4-(1-isopropyl-2-ethylimidazol-5-yl)-2-{4-[N-(2-methoxyethyl)sulphamoyl]anilino}  
 pyrimidine; and  
 4-(1-isopropyl-2-ethylimidazol-5-yl)-2-{4-[N-(2-ethoxyethyl)sulphamoyl]anilino} pyrimidine;  
 or a pharmaceutically acceptable salt or an *in vivo* hydrolysable ester thereof;
- 10    9.    A process for preparing a compound of formula (I) or a pharmaceutically acceptable  
 salt or an *in vivo* hydrolysable ester thereof which process (wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and p  
 are, unless otherwise specified, as defined in claim 1) comprises of:

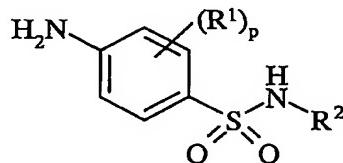
*Process a)* reaction of a pyrimidine of formula (II):



(II)

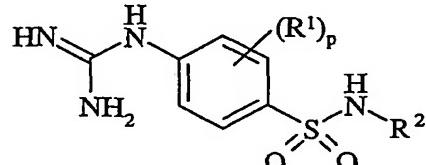
15

wherein L is a displaceable group; with an aniline of formula (III):



(III)

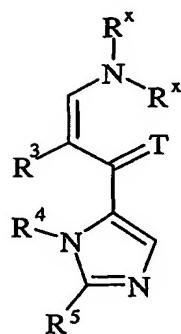
*Process b)* reacting a compound of formula (IV):



(IV)

20

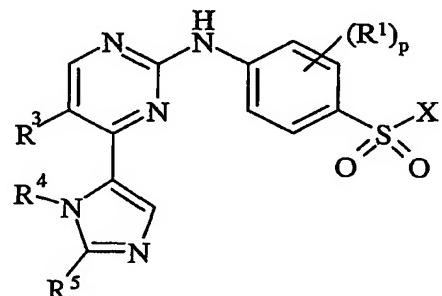
with a compound of formula (V):



(V)

wherein T is O or S; R<sup>x</sup> may be the same or different and is C<sub>1-6</sub>alkyl;

*Process c)* reacting a pyrimidine of formula (VI):



5

(VI)

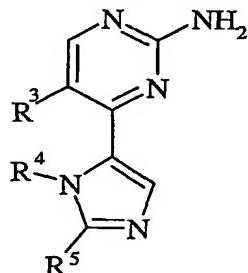
wherein X is a displaceable group; with an amine of formula (VII):



(VII)

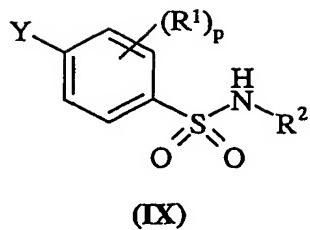
10 or

*Process d)* reacting a pyrimidine of formula (VIII)



(VIII)

with a compound of formula (IX):



where Y is a displaceable group;

and thereafter if necessary:

- 5    i) converting a compound of the formula (I) into another compound of the formula (I);  
 ii) removing any protecting groups;  
 iii) forming a pharmaceutically acceptable salt or *in vivo* hydrolysable ester.
  
- 10.   A pharmaceutical composition which comprises a compound of the formula (I), or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester thereof, according to any one of claims 1-8, in association with a pharmaceutically-acceptable diluent or carrier.
  
- 11.   A compound of the formula (I), or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester thereof, according to any one of claims 1-8, for use in a method of treatment of the human or animal body by therapy.
  
- 12.   A compound of the formula (I), or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester thereof, according to any one of claims 1-8, for use as a medicament.
  
- 20 13.   The use of a compound of the formula (I), or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester thereof, according to any one of claims 1-8, in the manufacture of a medicament for use in the production of a cell cycle inhibitory (anti-cell-proliferation) effect in a warm-blooded animal such as man.

14. The use of a compound of the formula (I), or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester thereof, according to any one of claims 1-8, in the manufacture of a medicament for use in the treatment of cancers (solid tumours and leukaemias), fibroproliferative and differentiative disorders, psoriasis, rheumatoid arthritis, Kaposi's sarcoma, haemangioma, acute and chronic nephropathies, atheroma, atherosclerosis, arterial restenosis, autoimmune diseases, acute and chronic inflammation, bone diseases and ocular diseases with retinal vessel proliferation.

5 15. The use of a compound of the formula (I), or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester thereof, according to any one of claims 1-8, in the manufacture of a medicament for use in the treatment of cancer.

10 16. The use according to claim 15 wherein the cancer is selected from leukaemia, breast cancer, lung cancer, colorectal cancer, stomach cancer, prostate cancer, bladder cancer, 15 pancreatic cancer, ovarian cancer, liver cancer, kidney cancer, skin cancer and cancer of the vulva.

17. A compound of the formula (I), or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester thereof, according to any one of claims 1-8, for use in the production of a 20 cell cycle inhibitory (anti-cell-proliferation) effect in a warm-blooded animal such as man.

18. A compound of the formula (I), or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester thereof, according to any one of claims 1-8, for use in the treatment of cancers (solid tumours and leukaemias), fibroproliferative and differentiative disorders, 25 psoriasis, rheumatoid arthritis, Kaposi's sarcoma, haemangioma, acute and chronic nephropathies, atheroma, atherosclerosis, arterial restenosis, autoimmune diseases, acute and chronic inflammation, bone diseases and ocular diseases with retinal vessel proliferation.

19. A compound of the formula (I), or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester thereof, according to any one of claims 1-8, for use in the treatment of 30 cancer.

20. A compound of the formula (I), or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester thereof, according to any one of claims 1-8, for use in the treatment of leukaemia, breast cancer, lung cancer, colorectal cancer, stomach cancer, prostate cancer, bladder cancer, pancreatic cancer, ovarian cancer, liver cancer, kidney cancer, skin cancer and  
5 cancer of the vulva.